

## LISTING OF CLAIMS:

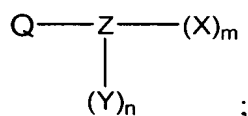
Please amend claims 2, 5, 6 and 175. This listing of claims replaces all prior versions and listings of claims in the application.

1. (Previously presented) A method for identifying non-targets of a drug, comprising:

(a) selecting a small organic molecule drug whose non-targets with which it interacts are to be identified, and providing a capture compound that presents the drug or a fragment, intermediate, metabolite or prodrug of the drug whose non-targets are to be identified, wherein:

the fragment, intermediate, metabolite or prodrug of the drug interacts with a non-target of the drug;

the capture compound has the formula:



X is a photoactivatable group that, upon exposure to light, covalently binds to an amino acid side chain of a protein to effect covalent binding of the capture compound to a protein;

Y is the small molecule organic drug or a fragment, intermediate, metabolite or prodrug thereof for assessing interactions with non-targets;

Q is a sorting function for immobilizing or separating the capture compounds;

Z is a trifunctional group containing 50 or fewer atoms that presents each of X, Y and Q;

m is 1; and

n is 1;

(b) contacting the capture compound with a sample containing non-target proteins that interact with Y, wherein contacting is effected under conditions in which X is not activated and for a sufficient time for interaction between the capture compounds and proteins in the sample to reach equilibrium, whereby Y interacts with drug non-target proteins in the sample;

(c) exposing the capture compound to electromagnetic radiation that activates X, whereby X forms a covalent linkage with protein(s) in the sample that are interacting with Y to effect capture thereof; and

(d) determining the identity of captured proteins, wherein the captured identified proteins comprise non-targets of the drug.

2. (Currently Amended) The method of claim 1, wherein Z comprises an amino acid; and Q a group for immobilizing or separating the capture compound comprises ~~selected from among~~ biotin, (His)<sub>6</sub>, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid ~~and~~ or an activated dextran.

3.-4. (Cancelled).

5. (Currently Amended) The method of claim 1, wherein steps (a)-(d) are performed a plurality of times, ~~method is performed a plurality of times,~~ each with the moiety Y is linked to the moiety Z in a different orientations via a different point ~~points~~ of attachments attachment on the Y moiety.

6. (Currently Amended) The method of claim 1, wherein:

X is selected from among an azide or a diazarine;

Z is an amino acid; and

Q is comprises biotin or an oligonucleotide.

7.-9. (Cancelled).

10. (Previously presented) The method of claim 1, wherein following step (a) or (c), the capture compounds are immobilized on a solid support via Q, which binds to the surface of the support or a molecule thereon.

11.-14. (Cancelled).

15. (Withdrawn) The method of claim 1, wherein:

Z is a moiety that is cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

16. (Cancelled).

17. (Previously Presented) The method of claim 1, wherein

Z is a moiety that is not cleavable prior to or during mass spectrometric analysis of biomolecules bound to the capture compound.

18. (Withdrawn) The method of claim 1, wherein:

Q is an oligonucleotide or oligonucleotide analog that includes a single-stranded portion of sufficient length "j" to form a stable hybrid with a base-complementary single stranded nucleic acid molecule or analog.

19.-21. (Cancelled).

22. (Withdrawn) The method of claim 1, wherein Q has the formula  $N^1_s B_i N^2_u$ , wherein:

$N^1$ , B and  $N^2$  are oligonucleotides or oligonucleotide analogs comprising s, t and u members, respectively;

B is a region of sequence permutations that contains at least two bases; and sum of s, i and u is at least 5.

23. and 24. (Cancelled).

25. (Original) The method of claim 1, wherein Z is a photocleavable, acid cleavable, alkaline cleavable, oxidatively cleavable, or reductively cleavable group.

26.-33. (Cancelled).

34. (Previously presented) The method of claim 1, wherein:

Q is selected from among biotin, (His)6, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran; and

Z has the formula:  $(S^1)_t M(R^{15})_a (S^2)_b L$ , wherein:

$S^1$  and  $S^2$  are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

$R^{15}$  is a monovalent group independently selected from  $Y^2 R^{18}$ ;

$Y^2$  is a divalent group independently having any combination of the following groups: a direct link, arylene, heteroarylene, cycloalkylene,  $>C(R^{17})_2$ ,  $C(R^{17})=C(R^{17})$ ,  $>C=C(R^{23})(R^{24})$ ,  $>C(R^{23})(R^{24})$ ,  $C\equiv C$ , O,  $>S(A)_u$ ,  $>P(D)_v(R^{17})$ ,  $>P(D)_v(ER^{17})$ ,  $>N(R^{17})$ ,  $>N(COR^{17})$ ,  $>N^+(R^{23})(R^{24})$ ,  $>Si(R^{17})_2$  and  $>C(E)$ ; where u is 0, 1 or 2; v is 0, 1, 2 or 3; A is O or  $NR^{17}$ ; D is S or O; and E is S, O or  $NR^{17}$ ;

$R^{17}$  and  $R^{18}$  are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro,  $SiR^{27}R^{28}R^{25}$ , alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl,

heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and  $\text{NR}^{19}\text{R}^{20}$ ;

$\text{R}^{19}$  and  $\text{R}^{20}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

$\text{R}^{23}$  and  $\text{R}^{24}$  are selected from (i) or (ii) as follows:

(i)  $\text{R}^{23}$  and  $\text{R}^{24}$  are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii)  $\text{R}^{23}$  and  $\text{R}^{24}$  together form alkylene, alkenylene or cycloalkylene;

$\text{R}^{25}$ ,  $\text{R}^{27}$  and  $\text{R}^{28}$  are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and  $\text{NR}^{19}\text{R}^{20}$ ;

$\text{R}^{15}$ ,  $\text{R}^{17}$ ,  $\text{R}^{18}$ ,  $\text{R}^{19}$ ,  $\text{R}^{20}$ ,  $\text{R}^{23}$ ,  $\text{R}^{24}$ ,  $\text{R}^{25}$ ,  $\text{R}^{27}$  and  $\text{R}^{28}$  can be substituted with one or more substituents each independently selected from  $\text{Z}^2$ ;  $\text{Z}^2$  is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy,  $\text{S}(\text{O})_h\text{R}^{35}$ ;  $h$  is 0, 1 or 2,  $\text{NR}^{35}\text{R}^{36}$ ,  $\text{COOR}^{35}$ ,  $\text{COR}^{35}$ ,  $\text{CONR}^{35}\text{R}^{36}$ ,  $\text{OC}(\text{O})\text{NR}^{35}\text{R}^{36}$ ,  $\text{N}(\text{R}^{35})\text{C}(\text{O})\text{R}^{36}$ , alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocyclyloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido;

$\text{R}^{35}$  and  $\text{R}^{36}$  are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylarylamino, diarylamino and arylamino; and

$\text{L}$  is a group that is cleavable prior to or during mass spectrometric analysis of the compound.

35.-37. (Cancelled).

38. (Original) The method of claim 34, wherein  $\text{L}$  is a disulfide moiety, a photocleavable group, an acid cleavable group, an alkaline cleavable group, a oxidatively cleavable group, or a reductively cleavable group.

39.-42. (Cancelled).

43. (Previously presented) The method of claim 34, wherein M is an amino acid and S<sup>1</sup> and S<sup>2</sup> each is independently (CH<sub>2</sub>)<sub>r</sub>, where r is 1-10.

44. (Previously presented) The method of claim 1, wherein an X is a diazirine, 3-trifluoromethyldiazirine or an azide; Z is an amino acid and Q is biotin.

45. (Cancelled).

46. (Cancelled).

47. (Withdrawn) The method of claim 1, wherein the capture compounds comprise a mass modifying tag linked to Z.

48.-54. (Cancelled).

55. (Withdrawn) The method of claim 18, wherein capture compounds are hybridized to a plurality of oligonucleotides or analogs thereof that comprise oligonucleotides that are complementary to each Q.

56. (Withdrawn) The method of claim 55, wherein the oligonucleotides or analog thereof that are complementary to Q are immobilized on a solid support as an array.

57.-62. (Cancelled).

63. (Withdrawn) The method of claim 1, wherein the Z moiety of the capture compound comprises a functionality conferring luminescence, fluorescence, chemiluminescence or colorimetric properties.

64. and 65. (Cancelled).

66. (Withdrawn) The method of claim 1, wherein the capture compounds further comprise a solubility group W that influences the solubility properties of the capture compound.

67. (Withdrawn) The method of claim 1, wherein the selectivity function Y is a drug or drug intermediate/fragment selected from among those set forth in Figure 17 and Figure 21.

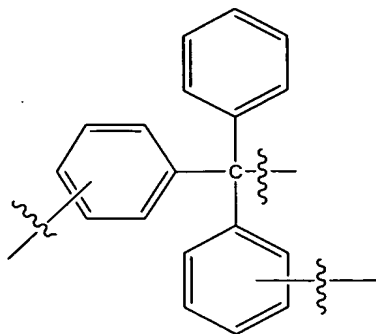
68. (Withdrawn) The method of claim 1, wherein the reactivity function X is selected from those set forth in Figure 16.

69.-74. (Cancelled).

75. (Previously presented) The method of claim 1, wherein Q is biotin.

76. (Cancelled).

77. (Withdrawn) The method of claim 1, wherein Z has the formula:



78.-109. (Cancelled).

110. (Previously presented) The method of claim 1, further comprising identifying or detecting a captured biomolecule by mass spectrometric analysis.

111.-115. (Cancelled).

116. (Previously presented) The method of claim 1, wherein the sample comprises a biological sample, a body tissue or fluid or a cell lysate.

117. (Cancelled).

118.-136. (Cancelled).

137. (Previously presented) The method of claim 1, wherein:

Q is selected from among biotin, (His)6, 4,4-difluoro-4-bora-3a,4a-diaza-s-indacene (BODIPY), an oligonucleotides, a nucleoside, a nucleotide, an antibody, an immunotoxin conjugate, an adhesive peptide, a lectin, a liposome, a peptide nucleic acid and an activated dextran; and

Z has the formula:  $(S^1)_t M(R^{15})_a (S^2)_b$ , wherein:

$S^1$  and  $S^2$  are spacer moieties;

t and b are each independently 0 or 1;

a is an integer from 0 to 4;

M is a central moiety possessing three or more points of attachment;

$R^{15}$  is a monovalent group independently selected from  $Y^2 R^{18}$ ;

$Y^2$  is a divalent group independently having any combination of the following groups:

a direct link, arylene, heteroarylene, cycloalkylene,  $>C(R^{17})_2$ ,  $C(R^{17})=C(R^{17})$ ,  $>C=C(R^{23})(R^{24})$ ,  $>C(R^{23})(R^{24})$ ,  $C\equiv C$ , O,  $>S(A)_u$ ,  $>P(D)_v(R^{17})$ ,  $>P(D)_v(ER^{17})$ ,  $>N(R^{17})$ ,  $>N(COR^{17})$ ,  $>N^+(R^{23})(R^{24})$ ,  $>Si(R^{17})_2$  and  $>C(E)$ ; wherein:

u is 0, 1 or 2;

v is 0, 1, 2 or 3;

A is O or  $NR^{17}$ ;

D is S or O; and

E is S, O or NR<sup>17</sup>;

R<sup>17</sup> and R<sup>18</sup> are each independently selected from the group consisting of hydrogen, halo, pseudohalo, cyano, azido, nitro, SiR<sup>27</sup>R<sup>28</sup>R<sup>25</sup>, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and NR<sup>19</sup>R<sup>20</sup>;

R<sup>19</sup> and R<sup>20</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heteroaralkyl and heterocyclyl;

R<sup>23</sup> and R<sup>24</sup> are selected from (i) or (ii) as follows:

(i) R<sup>23</sup> and R<sup>24</sup> are independently selected from the group consisting of hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl and heteroaryl; or

(ii) R<sup>23</sup> and R<sup>24</sup> together form alkylene, alkenylene or cycloalkylene;

R<sup>25</sup>, R<sup>27</sup> and R<sup>28</sup> are each independently a monovalent group selected from hydrogen, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy and NR<sup>19</sup>R<sup>20</sup>;

R<sup>15</sup>, R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup>, R<sup>23</sup>, R<sup>24</sup>, R<sup>25</sup>, R<sup>27</sup> and R<sup>28</sup> can be substituted with one or more substituents each independently selected from Z<sup>2</sup>; Z<sup>2</sup> is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, cycloalkenyl, hydroxy, S(O)<sub>h</sub>R<sup>35</sup>; h is 0, 1 or 2, NR<sup>35</sup>R<sup>36</sup>, COOR<sup>35</sup>, COR<sup>35</sup>, CONR<sup>35</sup>R<sup>36</sup>, OC(O)NR<sup>35</sup>R<sup>36</sup>, N(R<sup>35</sup>)C(O)R<sup>36</sup>, alkoxy, aryloxy, heteroaryl, heterocyclyl, heteroaryloxy, heterocyclyloxy, aralkyl, aralkenyl, aralkynyl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, aralkoxy, heteroaralkoxy, alkoxycarbonyl, carbamoyl, thiocarbamoyl, alkoxycarbonyl, carboxyaryl, halo, pseudohalo, haloalkyl and carboxamido; and

R<sup>35</sup> and R<sup>36</sup> are each independently selected from among hydrogen, halo, pseudohalo, cyano, azido, nitro, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkyl, alkenyl, alkynyl, haloalkyl, haloalkoxy, aryl, aralkyl, aralkenyl, aralkynyl, heteroaryl, heteroaralkyl, heteroaralkenyl, heteroaralkynyl, heterocyclyl, heterocyclylalkyl, heterocyclylalkenyl, heterocyclylalkynyl, hydroxy, alkoxy, aryloxy, aralkoxy, heteroaralkoxy, amino, amido, alkylamino, dialkylamino, alkylaryl amino, diarylamino and arylamino.

138. (Cancelled).

139. (Previously presented) The method of claim 137, wherein M is an amino acid.

140. (Previously presented) The method of claim 139, wherein X is an azide, S<sup>1</sup> and S<sup>2</sup> each is independently (CH<sub>2</sub>)<sub>r</sub>, where r is 1-10, and Q is biotin or an oligonucleotide.

141. and 142. (Cancelled).

143. (Withdrawn) The method of claim 1, further comprising re-designing the moiety Y to eliminate or alter its binding interactions with a captured biomolecule.

144. (Previously presented) The method of claim 1, further comprising identifying a function of a captured biomolecule.

145. (Withdrawn) The method of claim 143, wherein the alteration in binding is an increase in binding.

146. (Withdrawn) The method of claim 143, wherein the alteration in binding is a decrease in binding.

147. (Withdrawn) The method of claim 143, wherein the biomolecule for which binding is altered is a non-target biomolecule.

148.-150. (Cancelled).

151. (Previously presented) The method of claim 1, wherein the sample is contacted with a collection of capture compounds.

152. (Previously presented) The method of claim 1, wherein the X moiety of the capture compound comprises an azide, diazirine or a group which, following activation, reacts with the biomolecule.

153. (Withdrawn) The method of claim 143, wherein the method is repeated with the re-designed moiety Y linked to a capture compound to effect further modification thereof.

154. (Cancelled).

155. (Withdrawn) The method of claim 143, wherein the captured biomolecule for which binding is altered is a drug target protein.

156. (Withdrawn) The method of claim 143, wherein the captured biomolecule for which binding is altered is a non-drug target protein.

157.-159.(Cancelled).

160. (Previously presented) The method of claim 1, wherein a concentration of capture compound is varied in a plurality of different reactions.

161. (Previously presented) The method of claim 160, wherein a dissociation constant (K<sub>d</sub> value) is determined.

162. (Cancelled).



163. (Previously presented) The method of claim 110, wherein mass spectrometric analysis is performed using a mass spectrometric analysis format that is selected from among matrix assisted laser desorption ionization (MALDI), continuous or pulsed electrospray (ES) ionization, ionspray, thermospray, and massive cluster impact mass spectrometry.

164. (Previously presented) The method of claim 163, wherein the mass spectrometric analysis format is linear time-of-flight (TOF), reflectron time-of-flight, single quadrupole, multiple quadrupole, single magnetic sector, multiple magnetic sector, Fourier transform, ion cyclotron resonance (ICR), or ion trap.

165. (Cancelled).

166. (Previously presented) The method of claim 144, wherein the function of the biomolecule is determined by sequence alignment, pharmacophores, homology models and protein motif correlation, liver microsomes metabolic pathways, cDNA-expressed enzymes, signal pathways and back-mapping to yeast pathways, simulations and protein/protein interaction of pull-out proteins, native polymorphisms, knock-out/knock-in, flow cytometry, therapeutic activity of the drug, or prospective genotyping and prospective phenotyping.

167. (Withdrawn) The method of claim 143, wherein:  
the moiety Y is a first drug; and  
redesigning the first drug results in a second drug with fewer side-effects or an increased therapeutic index as compared to the first drug.

168. (Withdrawn) The method of claim 1, wherein the drug is selected from among troglitazone, rosiglitazone, pioglitazone, methotrexate, atorvastatin, celecoxib, refecoxib and cerivastatin.

169. (Previously presented) The method of claim 1, wherein the treatment comprises activation with light.

170. (Cancelled).

171. (Withdrawn) The method of claim 22, where B is a single stranded DNA or RNA and the number of sequence permutations is equal to  $4^i$ , wherein i is about 2 to about 25.

172. (Withdrawn) The method of claim 171, where i is about 3 to about 5, 6, 7 or 8.

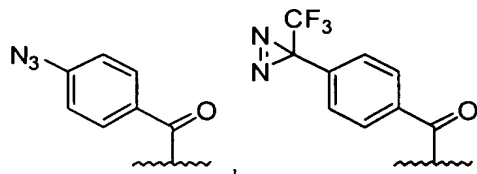
173. (Cancelled).

174. (Cancelled)

175. (Currently Amended) The method of claim 1, wherein X is

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Serial No. : 10/760,085  
Filed : January 16, 2004

Attorney's Docket No.: 3800014.00025/2309  
**Election and Response**



or an arylazide; Z is serine, threonine, lysine, tyrosine, glutamic acid, aspartic acid or cysteine; and Q is comprises biotin or an oligonucleotide.